REMARKS

Claims 19, 24, 25, 29 and 30 are pending in the application. Claim 29 has been amended. Support for the amendment is found in the specification at least at, *e.g.,* Figure 4, and the description of Figure 4 at page 13.

I. Rejection Under 35 U.S.C. § 103(a): Obata, Short, or Lihme

The Examiner has rejected claims 19, 24, and 25 under 35 U.S.C. § 103(a) as being unpatentable over the disclosure of Obata, taken in view of Short or Lihme. The Examiner contends that Obata teaches all elements of the invention with the exception that Obata does not use enzymes as a catalyst. The Examiner remedies this deficiency by the application of the disclosures of Short or Lihme, which allegedly teach use of biological enzymes in the bioconversion of potentially noxious substances, and water treatment wherein the active substance may be an enzyme respectively.

The applicants respectfully traverse the rejection.

The Examiner has failed to establish a *prima facie* case of obviousness. Obata teaches a method of producing pure water from urea-containing waste water. In the Obata process, once the water has been placed in the acidic softened water tank, it is tested and, if its pH is other than 3.0, the pH is adjusted using H_2O_2. Obata does not disclose consumption of water by humans, nor is there a disclosure of interference of urea in any "measurement results" allegedly obtained by the "human biosensor." Moreover, as the Examiner concedes, Obata provides no teaching of use of an enzyme in the Obata method of decomposing urea from waste water. Rather, the Obata catalyst is a platinum catalyst.

Short discloses a purified recombinant phytase derived from *E coli* having a specific structure and phytase activity. Short teaches that phytase enzymes, such as the claimed Short enzyme, are useful as supplements to phytate-containing foodstuffs, such as grains or legumes that are to be fed to non-ruminants, to avoid the difficulties associated with high production of fecal matter containing a high concentration of mineral and elements. The Short disclosure teaches that the recombinant phytase described can be used in a method of hydrolyzing phytates. Substrates for phytase include foodstuffs, potential foodstuffs, *ex vivo* reaction products and animal excrement products. Alternatively, Short teaches that the phytase may be administered to

a non-ruminant animal, for example, used in steeping cereals, the preparation of bread dough, and the preparation of sake.

Lihme teaches a fluidized bed chromatographic process for the purification and binding of molecules in a liquid to an active substance covalently bound to a chromatographic adsorbant particles. The active substance that is covalently bound to the particles may be an amino acid based polymer such as gelatin, albumen, hemoglobin, immunoglobin, antigens, G proteins, lectins, glycoproteins, biotin binding proteins, avadin, streptavadin enzymes, proteases, and protease inhibitors. In an aspect of the invention, the particles are floated in waste water in order to purify or at least partly purify the water. Lihme teaches that in such situations the floating aspect of the particles is significant, as it confers the advantage of oxygen being available for, *e.g.*, micro-organisms growing in the interior of the conglomerate.

The combination of Obata and Short or Lihme does not render obvious the claimed invention. First, the combination does not teach or suggest each element of the invention. Neither Obata-Short nor Obata-Lihme teaches or suggests a sample solution treating instrument having a control means for converting a sample solution to a condition for analysis by a biosensor that electrochemically measures a specific component in the sample solution. There is no biosensor disclosed in any of the three references. The Examiner contends that a human tasting water is interpreted as a biosensor in Obata. However, the applicants point out that there is no teaching of a human consuming water in Obata nor is there a teaching that such water is for human consumption. Additionally, a person tasting is not a process that electrochemically measures a specific component in water -- use of a human's gustatory apparatus is not the same as a measurement taken by the electrochemical means used in a biosensor.

Moreover, a person of skill in the art would not have had a motivation to combine the teachings of either Lihme or Short with those of Obata. Short teaches recombinant bacterial phytases which are to be used in the breakdown of phytates (phytic acids). Lihme provides only the general disclosure of "enzymes," but does not disclose use of the active substance covalently bound to chromatographic adsorbent particles, wherein the active substance is an enzyme for use in waste water treatment. Obata, in contrast, teaches use of a platinum catalyst for use in the breakdown of urea from waste water. Neither Lihme nor Short teaches removal or breakdown of urea using the phytases (Short), or the enzymes disclosed in Lihme (*e.g.*, glucose oxidase proteases). Neither phytases nor proteases nor glucose oxidases are used to decompose urea.

Thus, a person of skill in the art would have had no reason to make the combination of Obata with Lihme or Short, and therefore would have had no reasonable expectation that the combination would be successful, for it would not result in a process that was useful in the breakdown of urea.

Accordingly, for at least these reasons it is respectfully requested that the Examiner reconsider and withdraw the rejection based upon the combination of Obata and Short or Lihme.

II. Rejection Under 35 U.S.C. § 103(a): Yasuda

The Examiner has rejected claims 19 and 25 under 35 U.S.C. § 103(a) as being unpatentable over Yasuda. The Examiner contends that Yasuda teaches a method of measuring catecholamine including a sample pretreatment means and a sample dispensing means in the form of a syringe, which is coupled to the pretreatment means. The Examiner concedes that the reference does not teach that the sample pretreatment means is physically independent of the biosensor, but asserts that a person of skill in the art would have modified Yasuda by making the pretreatment means "separable" from the biosensing means.

The applicants respectfully traverse the rejection.

Yasuda discloses a method of detecting catecholamines, such as dopamines, norephinephrine, and epinephrine by fluorescent labeling. The detection method disclosed in Yasuda involves the steps of (1) obtaining a biological sample and adding, *inter alia,* maleimide to the sample prior to adding a fluorescence inducing reagent; subsequently adding a fluorescence reagent to the biological sample to obtain a "fluorescent inductor" (*i.e.*, a solution containing catecholamines with an activated fluophore); supplying the fluorescence inductor to a micro-syringe from which it is injected into a high speed liquid chromatographic device; and detecting the fluorescence intensity of the fluorescing catecholamines using a fluorometer.

Yasuda does not teach or suggest each element of the invention, for it does not describe a control means that includes an agent that is a catalyst or a buffer agent. When the sample solution is introduced into the micro-syringe (which the Examiner asserts is the control means), it already contains both the maleimide and the fluorescence inductor. Moreover, a person of ordinary skill in the art would not have been motivated to separate the micro-syringe from the fluorometer by detaching it from the tubing as suggested by the Examiner. The very purpose of the micro-syringe disclosed in Yasuda attached to the fluorometer is to ensure efficient and clean

waste free introduction of the sample into the fluorometer. A person of ordinary skill would not have been motivated, based on the disclosure of Yasuda, to place the sample syringe (already containing the maleimide and fluorescence inductor) into a syringe that is detached from the fluorometer and subsequently set up tubing between the micro-syringe and the fluorometer to inject the mixture into the fluorometer. Such a scenario is inefficient and a potentially wasteful process. There is no reason that the Examiner has pointed to that would have caused a person to undertake to do so in practicing the method of Yasudo.

Accordingly, it is submitted that the Examiner's rejection has been overcome. Its reconsideration and withdrawal is respectfully requested.

III. Rejection Under 35 U.S.C. § 103(a): Heller, Foulds, or Nankai

The Examiner has rejected claims 19 and 25 under 35 U.S.C. § 103(a) as being unpatentable over Heller, Foulds, or Nankai, each taken individually. The Examiner contends that although each admittedly discloses a biosensor coupled to the alleged control means, it would have been obvious to a person of skill in the art to modify each by separating the biosensor from the remaining apparatus.

The applicants respectfully traverse the rejection.

Heller discloses a biosensor having an electrode substantially covered by a "sensing layer" and, on top of the sensing layer, an "interferant eliminating layer," consisting of a catalyst that is capable of oxidizing, and thereby eliminating, interfering substances and a third outer layer that is "an oxidant generating layer." The Heller layered electrode may be placed in a cell into which a sample solution is added, or it may be inserted into the sample solution.

Foulds discloses a dry strip element to be used in an electrochemical assay method for detecting theophylline in human biological fluids. The element is made up of a working electrode and a reference electrode. At the working electrode is an alkaline phosphotase and an electroinactive phosphate ester. The dry strip element may also incorporate a buffer having a pH of nine to ten. The buffer is positioned between the region of the sample and the alkaline phosphotase. Foulds teaches that one may incorporate into the test element isozymes to remove any alkaline phosphotases indigenous to the sample that may reduce the desired substrate prior to the detection reaction, but that will not interfere with the detection reaction itself.

Nankai discloses an improved enzyme electrode that is made up of a first electrode having one or more enzymes immobilized upon it and a second electrode that functions to remove materials that may interfere with the detection method to be carried out by the first electrode. To accomplish the electrochemical detection using this electrode, both the first and the second electrode are submerged in the test solution. The second electrode serves to electrochemically oxidize any interfering substances as the detection is accomplished by the first electrode.

None of these references considered individually renders the claimed invention obvious. First, as the Examiner has conceded, none teaches or suggests each element of the invention as claimed. Each discloses an apparatus that is integral to that portion of the apparatus that carries out the detection or measurement reaction; thus, each is attached to the sensor or biosensor.

Moreover, a person of skill in the art would have had no motivation to make the modification suggested by the Examiner. First, in all three references, separation of the measurement/detection portion of the disclosed apparatus would either be technically non-productive, or would render the disclosed apparatus not useful for the application for which it was intended. In the case of Heller, the Heller interferant eliminating layer is sandwiched under the sensing layer and the oxidant generating layer. Separation of the bottom layer (the sensing layer) from the layered sandwiched electrode would disrupt the ordered treatment of the sample as it flows through the sandwiched electrode, and therefore destroy the aim of Heller. In the case of Foulds, the isozymes that remove undesirable alkaline phosphotases are incorporated within the material of the test strip. Separation of the isozymes from the test element would be infeasible and impracticable, and a person of skill would not have been motivated to do so. Similarly, Nankai focuses on dual electrodes in close proximity wherein the first electrode electrochemically oxidizes interfering substances as the sample flows to the second electrode. Similar to the situation in Heller, a person of ordinary skill would not have been motivated to separate the two electrodes, as separation would disrupt the desired sequence of pretreatments in Nankai.

For at least these reasons, a person of skill in the art would not have been motivated to make the modifications suggested by the Examiner of each of the above-discussed references. Accordingly, it is requested that the Examiner reconsider and withdraw the rejection.

IV. Rejection Under 35 U.S.C. § 103(a): Obata, Taken in View of Short or Lihme and Further in View of Blatt

The Examiner has rejected claim 29 under 35 U.S.C. § 103(a) as being unpatentable over Obata considered in view of Short or Lihme and taken further in view of Blatt. The Examiner applies Obata and Short or Lihme combination as discussed above, and adds the disclosure of Blatt for its alleged teaching of "an elastic sample supply means." The applicants respectfully traverse the rejection.

Obata, Short and Lihme are discussed above.

Blatt discloses a filter for effectively removing substances from a sample of bodily fluid. Blatt teaches that the Blatt filter can be incorporated into assay devices which use a wicking member or transport matrix that is a porous material through which the test sample can easily pass. Blatt discloses that the porous material may be a nylon pad for use in a pour and flow through assay device having multiple layers for multiple assay reagents. The Blatt pad is a sample pad to which the substance containing interfering substances is applied, prior to removal of the interfering substances by the filter of Blatt.

The combination suggested by the Examiner does not render obvious claim 29. The deficiencies and non-combinability issues raised above of Obata, Short, and Lihme are relied upon herein. Moreover, Blatt does not teach an elastic sample supply means. The nylon pad of Blatt for use in a pour and flow through assay device is a porous material. There is no suggestion or teaching in Blatt that it is elastic in nature. The Examiner asserts that the material "nylon" is inherently stretchable and therefore Blatt describes this element inherently. To the contrary, as would have been known to a person of ordinary skill in the art, the elasticity or stretchability of a given material such as nylon is determined by many factors, including the weave or configuration of the fibers composed of the chemical material, the size, shape, and other physical aspects of the arrangement of the fibers of the material and the material itself. Accordingly, there is no evidence that Blatt inherently teaches an elastic supply unit.

In addition, the pad in Blatt as referred to by the Examiner is not a "supply unit" within the meaning of claim 25. The pad in Blatt is used to accept the sample that still contains interfering material, prior to the filtering out of the interfering material by the pad. In contrast, the pad of the invention is where the sample is supplied to the biosensor -- by the time the

sample reaches the sample supply unit, any interfering compounds or substances have already been removed.

Therefore, for at least these reasons, it is respectfully requested that the Examiner reconsider and withdraw the rejection of claim 29 over this combination.

CONCLUSION

In view of the foregoing, it is respectfully submitted that claims 19, 24, 29 and 30 are patentable over the cited prior art. Reconsideration and allowance of all pending claims at the earliest opportunity is respectfully requested.

Respectfully submitted,

MARIKO MIYASHITA, *et al.*

7 June 2004 By: Kristyne A. Bullock
(Date)

KRISTYNE A. BULLOCK
Registration No. 42,371
AKIN GUMP STRAUSS HAUER & FELD LLP
One Commerce Square
2005 Market Street, Suite 2200
Philadelphia, PA 19103-7013
Telephone: 215-965-1200
Direct Dial: 215-965-1348
Facsimile: 215-965-1210
E-Mail: kbullock@akingump.com

KAB:cmb
7213292

Enclosures:
Petition for One Month Extension of Time
Request for Continued Examination